Published in final edited form as:
AIDS Care. 2008 March ; 20(3): 273–283. doi:10.1080/09540120701593489.

Using motivational interviewing to promote adherence to antiretroviral medications: A randomized controlled study

C. Dilorio[1], **F. McCarty**[1], **K. Resnicow**[2], **M. McDonnell Holstad**[3], **J. Soet**[1], **K. Yeager**[1], **S. M. Sharma**[4], **D. E. Morisky**[5], and **B. Lundberg**[6]

[1]Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory University, Atlanta, GA

[2]University of Michigan, Health Behavior & Health Education School of Public Health Ann Arbor, MI

[3]Nell Hodgson Woodruff School of Nursing, Emory University, Atlanta, GA

[4]Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA

[5]UCLA School of Public Health, Department of Community Health Sciences, Los Angeles, CA

[6]Consultant, Massachusetts, MA, US

Abstract

The primary aim of this study was to test an intervention to support antiretroviral medication adherence among primarily low-income men and women with HIV. The study was a randomized controlled trial (Get Busy Living) with participants assigned to treatment (Motivational Interviewing [MI]) and control groups. Participants were recruited from an HIV/AIDS clinic in Atlanta, Georgia, US. Of those referred to the study, 247 completed a baseline assessment and were enrolled with 125 randomized to the intervention group and 122 to the control group. Participants were patients beginning antiretroviral therapy or changing to a new drug regimen. The intervention consisted of five MI sessions delivered by registered nurses in individual counselling sessions. Participants were paid for each session attended. The intervention sought to build confidence, reduce ambivalence and increase motivation for ART medication-taking. Medication adherence was measured by the Medication Event Monitoring System (MEMS®) from the time of screening until the final follow-up conducted approximately 12 months following the baseline assessment. Participants in the intervention condition showed a trend towards having a higher mean percent of prescribed doses taken and a greater percent of doses taken on schedule when compared to the control group during the months following the intervention period. This effect was noted beginning at about the eighth month of the study period and was maintained until the final study month. Although the finding was weaker for overall percent of prescribed doses taken, the results for the percent of doses taken on schedule suggests that the MI intervention may be a

Correspondence: Professor Colleen DiIorio, PhD, RN, FAAN, Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory University, 1520 Clifton Rd, Room: 262, Atlanta, GA 30322, US. Tel: +1 (404) 727 8741. Fax: +1 (404)712 8872. cdiiori@sph.emory.edu.

useful approach for addressing specific aspects of medication adherence, such as adherrence to a specified dosing schedule.

Introduction

People infected with HIV face a number of challenges. One that has received considerable attention is medication adherence. The introduction of antiretroviral combination therapy (ART) in 1996 raised hopes for the control of HIV infection, but at the same time introduced an additional patient burden—managing a complex array of medications and associated behaviors. The consequences of non-adherence are high, as to reduce both viral load and the chance of developing opportunistic infections and drug-resistant mutations, people must take antiretroviral drugs exactly as prescribed, i.e. take the correct number of pills at the correct times each day under the appropriate conditions (Ickovics & Meade, 2002; Paterson et al., 2000). For antiretroviral medicines to exhibit optimal long-term benefits, people must maintain a high level of adherence over an indefinite period of time (Chesney et al., 1999; Paterson et al., 2000; Simoni et al., 2003). Adherence includes not only taking medications but often changes in lifestyle to accommodate medication-taking schedules and other requirements.

Because not all persons on ART take their medications exactly as prescribed and because there are serious consequences of non-adherence, there is a need to develop strategies to assist patients to meet these adherence challenges. Adherence strategies designed for persons with other types of chronic illness include education, reminders, self-monitoring, reinforcement, family support and behavioral interventions to enhance cognitive (self-efficacy and problem solving) and behavioral skills (Cooperman & Arnsten, 2005; Simoni et al., 2003). New and innovative strategies are also being considered, and the effectiveness of these approaches are now being tested in a variety of randomized clinical trials (Simoni et al., 2003). The purpose of this article is to report on one such study designed to test the efficacy of a counselling style—Motivational Inter-viewing—to promote adherence to ART. Motivational interviewing is a client-centered approach for enhancing motivation to change behavior or maintain healthy behaviors. The counselling strategy has been used successfully to modify a variety of behaviors, most notably drug and alcohol use (Miller & Rollnick, 2002)

Methods

Setting and design

Approval for the present study was obtained from the Institutional Review Board at Emory University and the Research Committee at the recruitment site. A Data Safety and Monitoring Board met regularly and reviewed the study data. No serious adverse events attributed to the intervention occurred during the study period. The study, named ‘Get Busy Living’, was conducted at an HIV/AIDS clinic, which is part of a large public medical centre serving a large southeastern metropolitan area. Over 4,000 men, women, adolescents and children with HIV are treated at the clinic each year. The study was a randomized controlled trial in which participants were randomized by use of computer-generated codes to either the usual care or intervention condition. Recruitment began June 2001 and continued to November 2003, with final assessments completed in January 2005.

Recruitment

Participants were recruited through nurse educators at the clinic. The population consisted of individuals who were prescribed ART for the first time or were changing medications and were referred to nurse educators for adherence education. The nurse educators assessed

patients for initial eligibility criteria, which was to be: (1) infected with HIV, (2) referred to the nurse educator for adherence education, (3) prescribed for the first time a multi-drug regimen or had a recent change in their regimen, (4) 18 years of age or older, (5) able to speak English and (6) willing to talk with a Get Busy Living recruiter. The nurse educators referred individuals meeting the above criteria to the Get Busy Living recruiter, who described the study to the person. Interested persons signed informed consent forms and completed a screening interview.

Study procedures

Participants who met eligibility criteria were given a MEMS® cap to monitor use of one medication in their ART regimen. Participants were instructed to use the MEMS® cap throughout the study period (12 months). To obtain baseline adherence data, participants used the MEMS® cap up to three weeks prior to completing a baseline assessment. Following the baseline assessment, they were randomly assigned to the control (usual care) group or the intervention group. Participants in the intervention group were scheduled for their first MI session with the study nurse counsellor, while those in the control group were scheduled for their first follow-up assessment three months after the baseline assessment. All participants were asked to return monthly to download data from their MEMS® caps and to return three times— at 3-, 6-, and 12-months post-baseline—to complete a questionnaire. These times were equivalent to two-weeks and three- and nine-months post-intervention for those in the intervention group. Participants completed all assessments using computer-assisted self-interviewing technology. In addition, face-to-face interviews were completed with a staff member to gather additional details about medications, including use of MEMS® caps, medication complexity and medication-taking during the previous four days, two weeks and 30 days. Participants were paid $25 for each assessment and received two tokens for public transport and a snack for coming to download the MEMS® caps (Figure 1).

Intervention

Participants in the intervention group received five individual MI counselling sessions with a study nurse counsellor over a 3-month period. The goal of these sessions was to help participants gain an understanding of their medication-taking behaviors and the actions necessary to successfully maintain a high level of adherence. To meet this goal, the counsellor used a MI script to guide the interaction with the participants. Motivational interviewing is a ‘client-centered directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence’ (Miller & Rollnick, 2002, p. 25). The communication style is reflected in a set of techniques to encourage participants to identify and discuss barriers to adherence, to express and resolve ambivalence about taking medications and to support motivation to attain or maintain adherence. In order to provide some standardization to the MI process, a semi-structured MI script was developed and used by the counsellors. The counsellor began by asking participants about their medication-taking behaviors over the past two weeks. For each medication, participants discussed their medication-taking behaviors, benefits and barriers of taking medications, and ways to improve their adherence. After each medication was discussed and an action plan developed, the counsellor ended each session by summarizing the discussion and the action plan agreed upon by the participant and counsellor. The majority (approximately 80%) of the sessions were held in person and lasted on average between 20 and 90 minutes with a median of 45, 35 and 30 minutes for sessions 1, 2 and 3–5, respectively. Session 1 was completed in-person for all participants. Telephone sessions (for sessions 2–5) were conducted as needed for participants who were unable to meet the counsellor in the clinic. For sessions 2–5, 17%, 21%, 15% and 16% were completed via telephone. All sessions were audio taped to assess fidelity to the intervention. Participants were paid $10 for completing the first MI session

and $5 for each of the remaining four sessions. In addition to the five MI sessions, participants in the intervention group received a copy of the Get Busy Living video, a journal and a calendar

Nurse counsellor training and monitoring

During the course of the study, 11 study nurses were trained in MI. The training, conducted by two of the authors (KR & JS), both psychologists trained in MI, included 24 hours of in-class presentations of theory and methods and practice sessions. Following these sessions, the nurses' skills were tested using a standardized patient approach (Ebbert & Connors, 2004). During the study, the MI nurses met every-other-week to discuss recent MI sessions and other relevant study issues. Periodic booster sessions were held to reinforce the MI techniques. To evaluate fidelity to the intervention, a psychologist and graduate students trained in MI counselling evaluated the MI tapes and coded them for fidelity using a structured coding form. These evaluations were used to assess MI nurses' adherence to the MI script and MI skills. Additional individualized training was provided for nurses to improve their skills as necessary. Overall, the evaluations showed that the nurses were adherent to the script and used appropriate MI skills during the MI sessions.

Control condition

Participants randomized to the control group received the usual adherence education provided at the clinic. Three nurse educators employed at the HIV clinic provide comprehensive adherence education to patients who are initiating or changing ART. They use a variety of teaching methods that are tailored for each individual based on factors such as education level, culture, type of regimen and time schedule. Each nurse educator makes the decision about his or her patient's readiness to begin taking ART. Eligible patients were referred to the Get Busy Living staff when the nurse educators cleared them to begin taking their medications. Participants could continue to meet with the nurse educators for adherence assistance as needed after the initial education sessions.

Measures

The Medication Event Monitoring System (MEMS® Caps, Aardex Ltd, Zug, Switzerland) was used as the primary measure of adherence and consists of a microprocessor that is contained within the cap of the medication bottle. When the cap is opened, the date and time of opening are recorded and stored. These data are downloaded to a computer and used to calculate a variety of adherence measures. For the present study, two MEMS® adherence rates were calculated. The first was based on the correspondence between the number of doses prescribed per day and the number of cap openings per day. The second was based on the number of cap openings occurring within ± one hour of the prescribed time for the dose. Each was converted to a percentage, i.e. percent of doses taken and percent of doses taken on schedule. Only one medication per person was monitored using MEMS®. The monitored medication was selected in the following order: (1) protease inhibitor (if two, then the one with the most complex dosing schedule), (2) non-nucleoside reverse transcriptase inhibitor and (3) reverse transcriptase inhibitor. The staff selected the medication for monitoring using a predetermined list of possible medication combinations. MEMS® caps have been used in a number of research studies assessing ART adherence and have been found to be a reliable and valid measure of adherence (Deschamps et al., 2004; Farley et al., 2003; Golin et al., 2002; Wagner, 2002; Wagner & Ghosh-Dastidar, 2002).

Data collected from the MEMS® cap event list were partitioned into two study phases: the time period two weeks prior to baseline (considered baseline adherence) and the time period from baseline to the 12-month assessment (study period adherence). For study period adherence, monthly adherence (4-week time blocks) was calculated for each participant

using all available data. Prior to generating the event list used to calculate the adherence rates, we also elected to non-monitor the following cap events: days with excessive openings (defined as ≥ 2 times the dosing schedule + 1), days when the cap was stored by the study staff due to patient being off medication, and days between the last download of a lost cap and the date of new cap receipt. Aside from these events, no other modifications were made to the MEMS® database.

To assess the secondary outcomes of the study, medical records of participants were reviewed for viral load and CD4 counts. The lab value along with the date was abstracted from the medical record. Viral load was measured by the AMPLICOR HIV-1 MONITOR® Test, v1.5 (Roche Molecular Systems, Inc., Alameda, CA). CD4 cell count was determined by the BD FACSCalibur™ system (BD Biosciences, San Jose, CA). All tests were conducted by the medical center laboratory, which used appropriate techniques to ensure reliability and validity of the results of the tests.

Data analyses

Preliminary analyses were conducted to identify group differences at baseline using independent samples *t*-tests and chi-square tests for continuous and categorical variables, respectively. We also examined the distribution of available adherence and lab data across the two groups (i.e. were the two groups contributing monthly data in a similar fashion?). Analyses were also conducted to investigate baseline differences among participants with ≤ 3 months, 4–6 months, and > 6 months of available adherence data. Similar analyses were conducted to compare baseline characteristics of those contributing two or fewer lab values to those with three or more for the first eight months of the study period.

Adherence outcomes were analyzed using the MIXED procedure implemented in SPSS version 15.0. The analysis implemented through this procedure allows for correlated data (repeated measures) and for missing values. In addition to this approach, the same analyses were conducted using the Generalized Estimating Equation (GEE) procedure also implemented in SPSS 15.0. This additional analysis was conducted to investigate the robustness of the findings across two procedures commonly used to analyze longitudinal data with missing observations. A model with one within-subject factor (study month) and one between-subject factor (intervention group) was specified. Based on preliminary analyses, basline depression score (CES-D) and an index of recent drug use (calculated using the drug use variables presented in Table I) were included as covariates for the adherence outcomes. Although not statistically different in the two groups, these two variables were related to adherence. The primary test of the intervention effect was the group × time interaction. Adjusted parameter estimates for each study month were computed along with the 95% confidence intervals (CIs) in order to further interpret a statistically significant group by time interaction. All primary outcome analyses are based on an intention-to-treat analysis, with individuals included in each condition regardless of how much of the intervention they received or used. Participants with missing adherence outcomes were included in the analyses without any type of replacement of missing values.

For a somewhat smaller sample of participants, the change in viral load (log, $n = 201$) and CD4 count ($n = 197$) for the first eight months of the study were analyzed using the procedures described above with time and group as the within and between factors, respectively. Because lab values were abstracted from medical records and did not necessarily correspond directly with participant assessment dates, lab values were assigned to study months corresponding to those used for the adherence outcomes. Time was counted starting from the baseline assessment date with each lab being assigned to a 4-week time period. Lab values beyond the eighth month of the study were not included in these analyses because lab data became increasingly sparse during the later half of the study period. Using

the above method, the median time elapsed (days) from baseline (time 0) for each time period (study month), 0 through 7, was 0, 28, 56, 84, 112, 142, 168, 194 days, respectively. For some participants, this method resulted in the identification of two lab dates within the specified time period. The last observed value for that participant was used for analysis.

Results

Study participation

As shown in Figure 1, Figure 369 men and women were referred to the study staff. Of these, 282 were screened for eligibility and 247 completed a baseline assessment and were enrolled in the study. Slightly more participants (n = 125) were randomized to the intervention group than to the control group (n = 122). A total of 23 participants actively withdrew, were withdrawn from the study at various points or died: 14 in the control and nine in the intervention group. Most of these participants had died (70%). Other reasons for withdrawal included: moved, time constraints and loss of interest. Because the primary measures of adherence were based on data obtained from MEMS® cap use, participants with at least one month (4 weeks) of monitored days beyond the date of baseline assessment were included in the main analyses (n = 213).

Table I presents the characteristics of the 213 study participants included in the main analyses. The participants ranged in age from 22–61 years with a mean age of 41 years. Most participants were male (65%), African American (89%) and single/never married (55%). While the majority had completed high school (86%), 83% were unemployed and 88% reported a monthly income of less than $1,200. The two groups were very similar on all demographic characteristics. Based on the results of independent samples t-tests and chi-square tests, the two groups were not statistically different ($p > 0.05$) on any variable assessed at baseline.

Analyses were also conducted to identify any differences between the two groups in terms of the number of adherence and lab data points provided by each participant. Of the 213 participants, 72% had adherence data for seven or more follow-up study months with 15% having data for 4–6 months and 13% having data for three or fewer months. On average, participants had nine months of adherence data. The MI and control groups did not differ on the number of adherence data points contributed by each participant. The analyses conducted to investigate baseline differences among participants with ≤ 3 months, 4–6 months and > 6 months of follow-up adherence data indicated that those contributing less data tended to have higher depression scores ($p < 0.05$) and be less adherent during the 2-week period prior to baseline ($p < 0.001$). Both of these variables have been included in the main analyses as covariates. The analyses conducted to identify differences between the groups with respect to the contribution of lab values for the first eight months of the study did not reveal any significant differences. For all participants, the mean number of labs contributed per participant was three for viral load and about 2.5 (median =2) for CD4 count. Although not statistically significant, a slightly higher percent of those in the control group (66%) contributed three or more lab values compared to the MI group (57%). In a comparison of baseline values for those with ≥ 3 available labs and those with < 3, only one difference ($p = 0.051$) was noted: a higher percent of females (71%) had three or more labs compared to males (56%). This difference was consistent across the two groups.

Adherence outcome

For the primary analysis, the MEMS® data from 213 participants were analyzed using a mixed model approach with repeated measures. The results of tests of fixed effects (group, time and group by time) for each outcome are reported in Table II along with the unadjusted

estimated means and 95%CIs for selected time points. For the percent of prescribed doses outcome, the group by time interaction was statistically significant. While the time main effect was statistically significant, the group main effect was not. The estimated adjusted means for the group by time effect are displayed in Figure 2. Based on the CIs for the percent of doses taken, the intervention and control groups do not appear to be statistically different at most of the time points during the study. However, the intervention group appears to diverge somewhat from the control group during the later months of the study.

For the percent of prescribed doses taken on schedule variable, the group by time effect was statistically significant. The time and group main effects were also statistically significant. The estimated means for the group by time effect are displayed in Figure 3. For this outcome there are clear non-overlapping MI and control group CIs during both the intervention and follow-up periods, with the MI and control group difference becoming wider towards the later part of the follow-up period.

The analysis of viral load (log value) resulted in no statistically significant effects. The same was true for CD4 count. Given the somewhat non-normal distribution of the viral load log, we decided to convert this variable to a binary variable with 1 being undetectable (viral load ≤0.40) and 0 detectable (viral load >0.40). Analyses of this variable resulted in a significant main effect for time with the only significant increase in the proportion of participants with an undetectable viral load occurring from baseline to the first study month. The estimated means and 95%CIs for these variables are reported in Table II. These results should be interpreted with caution as the timing of labs was highly variable and not under the control of the study.

Discussion

The primary aim of the study was to test an intervention designed to improve adherence among people taking antiretroviral medications. This study was among the first to provide a rigorous test of the use of MI for antiretroviral medication adherence and also among the first to train nurses to deliver the MI intervention for antiretroviral adherence. The results showed that during the follow-up period, participants in the intervention group were taking a greater percentage of their prescribed doses and a significantly greater percentage of doses on time compared to those in the control group. Although no intervention effect was noted for the lab results, viral load tended to be a little lower in the intervention group. Overall, all study participants showed a general improvement in lab values over the course of the study period.

These findings provide evidence to support the usefulness of MI in promoting antiretroviral medication adherence and add to the previous studies in the area. The results of two pilot studies provided preliminary evidence that MI counselling methods could be used to support the adherence efforts of men and women taking antiretroviral medications (DiIorio et al., 2003; Parsons et al., 2005). The results of the current study provide additional evidence for a client-centered approach that seeks to increase intrinsic motivation and reduce ambivalence for medication adherence.

Not all studies, however, have shown MI to be more efficacious than usual adherence education in the clinical setting. Samet et al. (2005) found no difference in self-reported adherence between participants assigned to an MI intervention group and those assigned to the usual care group. Participants (n = 151) in their study were limited to men and women who had a history of alcohol problems. Although the intervention was similar (four MI encounters versus our five MI sessions and both interventions delivered by a nurse trained in MI), the assessment of adherence was different. We compared the percentage of doses taken

using MEMS® caps, whereas Samet et al. used self-reported measures that were corroborated with data from MEMS® caps. The researchers also noted that sample size and limited exposure to the intervention for some participants may have been factors in the failure to detect differences between groups.

The MI communication style is used primarily by counsellors and psychologists in their clinical practices. However, in the HIV clinical setting, registered nurses (RN) are most often responsible for adherence education and counselling. Thus, in our study, RNs were trained in MI skills and delivered the intervention. In an early study, Stott et al. (1996) trained physicians and nurses to deliver brief MI-based counselling sessions to patients with diabetes. The results of this study and the present study provide evidence for the value of incorporating the MI communication style into the clinical practice of nurses, and studies such as these may increase its acceptability among nurses. The median time for MI sessions in the present study ranged from 30–45 minutes, which is longer than a usual clinical appointment with a healthcare provider. However, in many HIV clinics, nurses specialize in providing ART adherence education for patients. In these centers, nurses can use MI as one approach to support adherence. Additional studies can examine the incorporation of the MI approach as a brief ART adherence intervention conducted within the context of the office visit.

The percent of adherence recorded for participants in this study and the pattern of adherence over time were comparable to those reported in other studies. At baseline, participants took, on average, 80% of the prescribed doses of medication and, on average, 58% of the medication on time. One year later, participants took an average of 60% of the doses with about 32% on time. Although direct comparisons are difficult because of varying time periods used to calculate adherence rates, other investigators have reported MEMS®-based adherence rates that are comparable to the ones found in this study (Liu et al., 2001). Other investigators have also noted a decline in adherence over time. For example, Remien et al. (2005) reported adherence rates of 75% and 66% at baseline and 6-month follow-up for their intervention group participants with similar values for the control group. Liu et al. (2001) also reported a downward change over time in MEMS®-based adherence rates.

In this study, the pattern of decline was different for the intervention and control groups. For both groups, the percent of adherence declined during the first three months. The decline continued for those in the control group, while it was attenuated for those in the intervention group. That attenuation was noted for both the percent of doses taken and the percent of doses taken on time is an interesting finding and suggests long-term effects of the MI intervention. One goal of MI is to increase intrinsic motivation for behavioral change. People who rely on intrinsic motivation as opposed to extrinsic motivation to support health behaviors are more likely to persevere in the face of difficulties (Ryan & Deci, 2000). One explanation for the attenuation seen in the present study may be that participants in the intervention group relied upon what they learned in the MI intervention sessions to motivate themselves to take their medications. Further research is necessary to evaluate the long-term outcomes associated with MI.

Limitations

There are several limitations of this study. First, the sample was composed primarily of low-income African American men. Thus, the results cannot be generalized to those in other groups who are also prescribed ART. Future research should focus on other groups affected by HIV, including women and gay men and other cultural groups, including Hispanic and Asian men and women. Second, all men and women who were initiating or changing ART were eligible to participate provided they met other study criteria. We did not limit participants to those who were reported difficulties taking their medications. We found that

many participants maintained a high level of adherence throughout the study, limiting our ability to fully test the usefulness of MI in promoting behavioral change. Finally, we asked participants to use MEMS® caps throughout the one-year study. This proved difficult for some individuals. In future studies, researchers might consider limiting the use of these caps to short periods of time around the follow-up assessment periods. Finally, cost of lab tests limited our ability to fully test the effect of the intervention on viral load and CD4 counts. Although there was some indication that those in the intervention group had more favorable lab values, future research should include systematic assessment of these indices. Finally, the types and doses of medications changed over the course of the study. Overall, these changes were made to reduce medication burden. The extent to which these types of changes influence medication adherence and the need for adherence support should be examined in future research.

Acknowledgments

This study was funded by a grant from the National Institute of Nursing Research R01 NR04857. We wish to acknowledge the assistance of the Infectious Disease Program in the conduction of this study. We appreciate the assistance of the staff and the contributions of the participants who enrolled in the study.

References

Chesney MA, Ickovics J, Hecht FM, Sikipa G, Rabkin J. Adherence: A necessity for successful HIV combination therapy. AIDS. 1999; 13 Suppl. A:S271–S278. [PubMed: 10885784]

Cooperman NA, Arnsten JH. Motivational interviewing for improving adherence to antiretroviral medications. Current HIV/AIDS Reports. 2005; 2:159–164. [PubMed: 16343372]

Deschamps AE, Graeve VD, van Wijngaerden E, De Saar V, Vandamme A, van Vaerenbergh KV, et al. Prevalence and correlated of non-adherence to antiretroviral therapy in a population of HIV patients using Medication Event Monitoring System. AIDS Patient Care and STDs. 2004; 18:644–657. [PubMed: 15633262]

DiIorio C, Resnicow K, McDonnell M, Soet J, McCarty F, Yeager K. Using motivational interviewing to promote adherence to antiretroviral medications: A pilot study. Journal of the Association of Nurses in AIDS Care. 2003; 14:52–62. [PubMed: 12698766]

Ebbert DW, Connors H. Standardized patient experiences: Evaluation of clinical performance and nurse practitioner student satisfaction. Nursing Education Perspectives. 2004; 25:12–15. [PubMed: 15017794]

Farley J, Hines S, Musk A, Ferrus S, Tepper V. Assessment of adherence to antiviral therapy in HIV-infected children using the Medication Event Monitoring system, pharmacy refill, provider assessment, caregiver self-report and appointment keeping. Journal of AIDS. 2003; 33:211–218. [PubMed: 12794557]

Golin CE, Liu H, Hays RD, Miller LG, Beck CK, Ickovics J, et al. A prospective study of predictors of adherence to combination antiretroviral medication. Journal of General Internal Medicine. 2002; 17:756–765. [PubMed: 12390551]

Ickovics JR, Meade CS. Adherence to antiretroviral therapy among patients with HIV: a critical link between behavioral and biomedical sciences. Journal of Acquired Immune Deficiency Syndromes. 2002; 31 Suppl. 3:S98–S102. [PubMed: 12562029]

Liu H, Golin CE, Miller LG, Hays RD, Beck CK, Sanandaji S, et al. A comparison study of multiple measures of adherence to HIV protease inhibitors.[see comment][erratum appears in *Annals of Internal Medicine, 136*, 175]. Annals of Internal Medicine. 2001; 134:968–977. [PubMed: 11352698]

Miller, RW.; Rollnick, S. Motivational interviewing: Preparing people for change. 2nd edition. New York: Guilford Press; 2002.

Parsons JT, Rosof E, Punzalan JC, Di Maria L. Integration of motivational interviewing and cognitive behavioral therapy to improve HIV medication adherence and reduce substance use among HIV-

positive men and women: Results of a pilot project. AIDS Patient Care & STDs. 2005; 19:31–39. [PubMed: 15665633]

Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection.[see comment][erratum appears in *Annals of Internal Medicine, 136*, 253]. Annals of Internal Medicine. 2000; 133:21–30. [PubMed: 10877736]

Remien RH, Stirratt MJ, Dolezal C, Dognin JS, Wagner GJ, Carballo-Dieguez A, et al. Couple-focused support to improve HIV medication adherence: A randomized controlled trial. AIDS. 2005; 19:807–815. [PubMed: 15867495]

Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development and well-being. American Psychologist. 2000; 55:68–78. [PubMed: 11392867]

Samet JH, Horton NJ, Meli S, Dukes K, Tripps T, Sullivan L, et al. A randomized controlled trial to enhance antiretroviral therapy adherence in patients with a history of alcohol problems. Antiviral Therapy. 2005; 10:83–93. [PubMed: 15751766]

Simoni JM, Frick PA, Pantalone DW, Turner BJ. Antiretroviral adherence interventions: A review of current literature and ongoing studies. Topics in HIV Medicine. 2003; 11:185–198. [PubMed: 14724327]

Stott NC, Rees M, Rollnick S, Pill RM, Hackett P. Professional responses to innovation in clinical method: Diabetes care and negotiating skills. Patient Education & Counselling. 1996; 29:67–73.

Wagner GJ. Predictors of antiretroviral adherence as measured by self-report, electronic monitoring and medication diaries. AIDS Patient Care and STDs. 2002; 16:599–608. [PubMed: 12542933]

Wagner GJ, Ghosh-Dastidar B. Electronic monitoring: Adherence assessment or intervention? HIV Clinical Trials. 2002; 3:45–51. [PubMed: 11819185]

Figure 1.
Flowchart of study recruitment, allocation and retention.

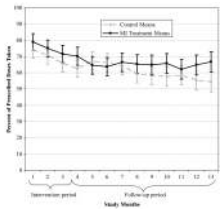

Figure 2.
Estimated group by time means for percent of prescribed doses taken with 95%CI error bars. Covariates: baseline percent of doses taken on schedule = 83, CES-D =14, baseline drug use = 1.9.

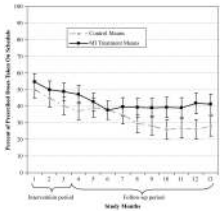

Figure 3.
Estimated group by time means for percent of prescribed doses taken on schedule (within ±1 hour) with 95%CI error bars. Covariates: baseline percent of doses taken on shedule = 62; CES-D =14; baseline drug use = 1.9.

Table I

Descriptive statistics for personal characteristics of participants in the intervention and control groups.

Variable	MI *n* = 107	Control *n* = 106	Total *n* = 213
Age			
Mean (SD)	41 (6.9)	41 (7.4)	41.6 (7.1)
Gender (%)			
Male	66	64	65
Female	34	32	33
Transgender		4	2
Race (%)			
African American	92	86	89
White	6	7	7
Other	2	7	4
Marital status (%)			
Never married	53	57	55
Separated/divorced/widowed	26	29	28
Married/committed relationship	21	14	17
Education (%)			
< High school	15	13	14
High school	49	54	51
> High school	36	33	35
Paid employment (%)			
Yes	18	16	17
Sexual identity (%)			
Straight, heterosexual	48	53	50
Gay, homosexual	33	26	30
Bisexual	10	8	9
None of the above/unsure	9	13	11
Have children (%)			
Yes	51	51	51
Monthly income (%)[a]			
<$500	34	27	31
501–750	40	40	40
751–950	6	14	10
951–1,150	10	6	8
1,151–6,000	10	13	11
How often do you drink alcohol? (%)			
Never	59	56	57
1–3 ×/month	26	26	26
1 or 2 ×/week	8	11	10
3 or more ×/week	7	7	7
Drug use in the past 6 months % current (number ever used)			

Variable	MI *n* = 107	Control *n* = 106	Total *n* = 213
Marijuana	25 (*n* = 89)	33 (*n* = 80)	28 (*n* = 169)
Cocaine	36 (*n* = 70)	40 (*n* = 78)	38 (*n* = 148)
Heroin	0 (*n* = 15)	10 (*n* = 20)	6 (*n* = 35)
Amphetamines/speed	10 (*n* = 29)	0 (*n* = 30)	5 (*n* = 59)
CES-D total score	14.7 (10.4)	13.9 (9.8)	14.3 (10.1)
Baseline percent of prescribed doses taken			
Mean (SD)	79.1 (25.9)	80.2 (20.8)	79.7 (23.0)
Baseline percent of prescribed doses taken on schedule			
Mean (SD)	58.1 (32.5)	57.6 (30.8)	57.8 (31.6)
Viral load[b]			
Mean (SD) (copies per ml × 1000)	11.0 (21.9)	9.2 (19.9)	
Viral load (log)			
Mean (SD)	3.3 (0.79)	3.3 (0.72)	
CD4 count[c]			
Mean (SD)	250.3 (192.5)	243.0 (183.1)	

[a] MI Intervention *n* = 97, Control *n* = 97.

[b] MI Intervention *n* = 99, Control *n* = 90.

[c] MI Intervention *n* = 79, Control *n* = 70.

Table II

Results from tests for fixed effects and unadjusted estimated means and 95%CI by group for selected time points.

	Study month				Fixed effects *p*-values					
					Group		Time		Group ×Time	
Outcome	0 Mean (95%CI)	3 Mean (95%CI)	6 Mean (95%CI)	12 Mean (95%CI)	MIXED	GEE	MIXED	GEE	MIXED	GEE
Percent of prescribed doses taken					.090	.111	<.001	<.001	.023	.013
MI group	79 (74, 85)	70 (64, 76)	63 (57, 68)	64 (57, 70)						
Control group	80 (75, 86)	65 (59, 71)	66 (60, 72)	55 (49, 62)						
Total	80 (76, 84)	68 (64, 72)	64 (60, 68)	60 (55, 64)						
Percent of prescribed doses taken on schedule					.004	.006	<.001	<.001	.005	.040
MI group	58 (53, 64)	47 (41, 53)	36 (30, 43)	41 (34, 47)						
Control group	57 (51, 63)	38 (32, 44)	35 (29, 42)	24 (18, 31)						
Total	58 (54, 62)	43 (38, 47)	36 (31,40)	32 (28, 37)						
Viral load (log)					.165	.172	.627	.539	.806	.835
MI group	3.29 (3.10, 3.48)	3.13 (2.87, 3.38)	3.05 (2.79, 3.32)							
Control group	3.35 (3.15, 3.55)	3.15 (2.93, 3.38)	3.39 (3.13, 3.65)							
Total	3.32 (3.18, 3.46)	3.14 (2.97, 3.31)	3.22 (3.04, 3.41)							
Viral load-percent of participants undetectable						.410		<.001		.970
MI group	27% (16, 38)	59% (43, 76)	58% (41, 76)							
Control group	20% (10, 30)	60% (48, 73)	47 (31, 64)							
Total	23% (16, 31)	60% (49, 70)	53% (41, 65)							
CD4 Count					.943	.937	.025	.077	.757	.687
MI group	235 (195, 276)	240 (195, 285)	227 (180, 274)							

	Study month				Fixed effects *p*-values					
					Group		Time		Group ×Time	
Outcome	0 Mean (95%CI)	3 Mean (95%CI)	6 Mean (95%CI)	12 Mean (95%CI)	MIXED	GEE	MIXED	GEE	MIXED	GEE
Control group	235 (192, 277)	242 (199, 286)	262 (214, 310)							
Total	235 (206, 264)	241 (210, 272)	244 (210, 278)							